

CLAIMS

Sub E1

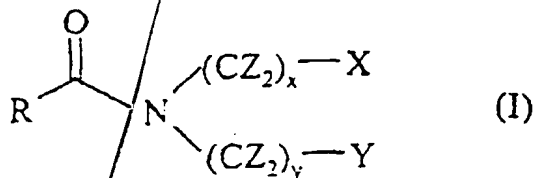
1. Agents for transferring nucleic acids, characterized in that they comprise a hydrophobic spacer chemically linked, firstly, to a polycation and, secondly, to at least one hydrophilic substituent.

2. Agents for transferring nucleic acids according to Claim 1, characterized in that said hydrophobic spacer consists of 2 or 3 hydrocarbon-based linear fatty chains comprising between 10 and 20 carbon atoms per chain, each chain possibly being of different length, or of said hydrophobic spacer consists of a very long hydrocarbon-based linear fatty chain comprising between 20 and 50 carbon atoms.

3. Agents for transferring nucleic acids according to Claim 1, characterized in that the hydrophilic substituent(s) is (are) chosen from hydroxyl or amino substituents, polyols, sugars or hydrophilic peptides.

4. Agents for transferring nucleic acids according to Claim 1 or 3, characterized in that at least one of the hydrophilic substituents is a sugar.

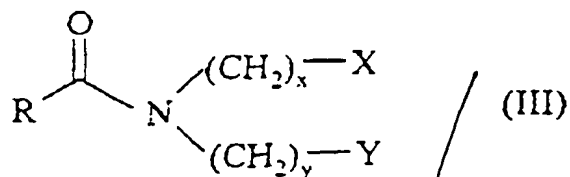
5. Agents for transferring nucleic acids according to Claim 1, of general formula (I):



for which:

- R represents a polycation,
- Z represents a hydrogen atom or a fluorine atom, the various Zs being independent of each other, and
- 5 - either x and y, independently of each other, represent integers between 10 and 22 inclusive, and X and Y, independently of each other, represent a hydrogen atom, an -OAlk group in which Alk represents a straight or branched alkyl containing 1 to 4 carbon
- 10 atoms, a hydroxyl group, an amino group, a polyol, a sugar, a hydrophilic or non-hydrophilic peptide, or an oligonucleotide, it being understood that at least one of the X and Y substituents represents a hydrophilic group chosen from hydroxyl groups, amino groups,
- 15 polyols, sugars or hydrophilic peptides,
- or x is equal to 0 or 1, y is an integer between 20 and 50, X is either a hydrogen atom or an -OAlk group in which Alk represents a straight or branched alkyl containing 1 to 4 carbon atoms, and Y is a hydrophilic
- 20 group chosen from hydroxyl groups, amino groups, polyols, sugars or hydrophilic peptides,
- where appropriate in the isomeric forms thereof, and also the mixtures thereof or the salts thereof, when they exist.

25                   6.    Agents for transferring nucleic acids according to Claim 1 or 5, of general formula (III):



for which:

- R represents a polycation, and
- 5 - either x and y, independently of each other, represent integers between 10 and 22 inclusive, and X and Y, independently of each other, represent a hydrogen atom or a sugar, it being understood that at least one of the X and Y substituents represents a
- 10 sugar,
- or x is equal to 0 or 1, y is an integer between 20 and 50, X is a hydrogen atom and Y is a sugar, where appropriate in the isomeric forms thereof, and also the mixtures thereof or the salts thereof, when
- 15 they exist.

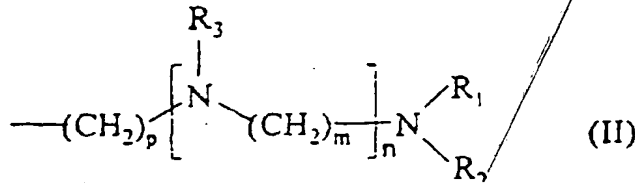
7. Agents for transferring nucleic acids according to Claim 6, characterized in that x and y, independently of each other, represent integers between 10 and 22 inclusive, and one of X and Y represents a

20 hydrogen atom and the other a sugar.

8. Agents for transferring nucleic acids according to one of Claims 1 and 5 to 7, characterized in that said polycation is a linear or branched polyamine, each amino group being separated by one or

25 more methylene groups.

9. Agents for transferring nucleic acids according to Claim 8, characterized in that said polycation has the general formula (II):



in which:

- $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  represent, independently of each other, a hydrogen atom or a  $(\text{CH}_2)_q\text{NR}'\text{R}''$  group with  $q$  an integer possibly ranging from 1 to 6, this being independent among the various  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  groups, it being understood that at least one of  $\text{R}_1$ ,  $\text{R}_2$  and  $\text{R}_3$  is other than a hydrogen atom,
- $\text{R}'$  and  $\text{R}''$  represent, independently of each other, a hydrogen atom or a  $(\text{CH}_2)_q\text{NH}_2$  group with  $q$  defined as above,
- $m$  represents an integer between 1 and 6, and
- $n$  and  $p$  represent, independently of each other, integers between 0 and 6, with, when  $n$  is greater than or equal to 2,  $m$  being able to have different values and  $\text{R}_3$  different meanings within the general formula (II) and, when  $n$  is equal to 0, at least one of the  $\text{R}_1$  and  $\text{R}_2$  substituents is other than a hydrogen atom.

10. Agents for transferring nucleic acids according to one of Claims 1 and 5 to 7, characterized

in that said polycation is chosen from spermine,  
spermidine, cadaverine, putrescine,  
hexamethylenetetramine (hexamine),  
methacrylamidopropyltrimethylammonium chloride

5 (AMBTAC), 3-acrylamido-3-methylbutyltrimethylammonium  
chloride (AMBTAC), polyvinylamines, polyethyleneimines,  
or ionenes.

E  
11. Agents for transferring nucleic acids  
according to one of Claims 3 to 7, characterized in  
10 that the sugar(s) is (are) a molecule or molecules of  
mono-, oligo- or polysaccharide.

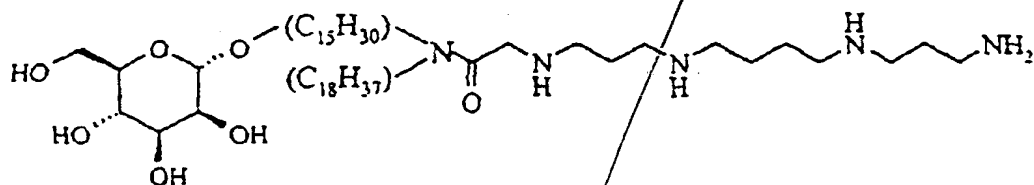
12. Agents for transferring nucleic acids  
according to Claim 11, characterized in that said  
sugar(s) is (are) chosen from glucose, mannose,  
15 rhamnose, galactose, fructose, maltose, lactose,  
saccharose, sucrose, fucose, cellobiose, allose,  
laminarabiose, gentiobiose, sophorose, melibiose,  
dextran,  $\alpha$ -amylose, amylopectin, fructans, mannans,  
xylans and arabinans.

20 13. Agents for transferring nucleic acids  
according to Claim 5, characterized in that said  
oligonucleotide is any chain containing one or more  
nucleotides, deoxynucleotides, ribonucleotides and/or  
deoxyribonucleotides, optionally coupled to one or more  
25 molecules having distinct properties.

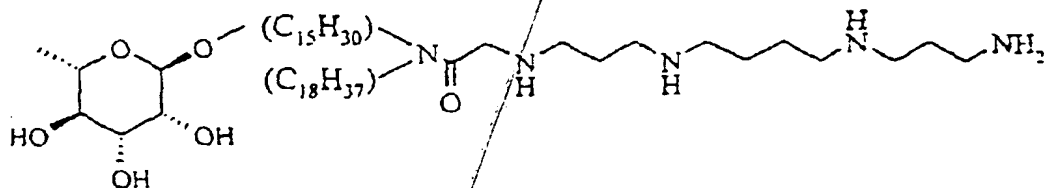
14. Agents for transferring nucleic acids  
according to Claim 5, characterized in that said

peptide is any chain containing one or more amino acids linked to each other via attachments of a peptide nature, optionally substituted with one or more aliphatic groups which may be saturated or unsaturated, and linear, branched or cyclic.

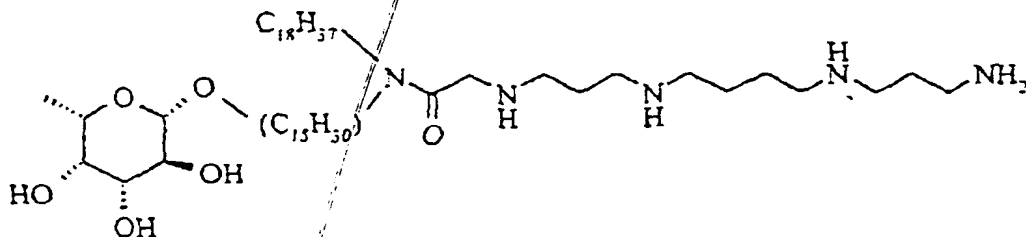
15. Transfer agent according to Claim 1, of formula:



16. Transfer agent according to Claim 1, of formula:



17. Transfer agent according to Claim 1, of formula:



18. Composition characterized in that it contains an agent for transferring nucleic acids as defined in Claims 1 to 17, and a nucleic acid.

19. Composition according to Claim 18, characterized in that the nucleic acid is a deoxyribonucleic acid or a ribonucleic acid.

20. Composition according to Claim 18 or 19, characterized in that said nucleic acid comprises one or more genes of therapeutic interest under the control of regulatory sequences.

21. Composition according to Claims 18 to 20, characterized in that said nucleic acid is an antisense sequence or gene.

22. Composition according to Claim 18, characterized in that it also contains one or more adjuvants.

23. Composition according to Claim 22, characterized in that the adjuvant is one or more neutral lipids.

24. Composition according to Claim 23, characterized in that the neutral lipids are lipids containing two fatty chains.

25. Composition according to Claims 23 and 24, characterized in that the neutral lipids are natural or synthetic lipids, which are zwitterionic or lacking ionic charge under physiological conditions, chosen, for example, from dioleoylphosphatidylethanolamine (DOPE), oleylpalmitoylphosphatidylethanolamine (POPE), di-stearoyl, -palmitoyl, -myristoylphosphatidyl-

ethanolamines and also the derivatives thereof which are N-methylated 1 to 3 times, phosphatidylglycerols, diacylglycerols, glycosyldiacylglycerols, cerebrosides (such as in particular galactocerebrosides),

5 sphingolipids (such as in particular sphingomyelins) or asialogangliosides (such as in particular asialoGM1 and GM2).

*E1*  
*conv*  
10 26. Composition according to Claim 22, characterized in that said adjuvant is a compound which is involved directly or indirectly in the condensation of the nucleic acid.

27. Composition according to Claim 26, characterized in that said adjuvant is derived, as a whole or in part, from a protamine, from a histone or  
15 from a nucleolin, and/or from a derivative thereof, or consists, as a whole or in part, of peptide units (KTPKKAKKP) and/or (ATPAKKAA), the number of units possibly ranging between 2 and 10, and possibly being repeated continuously or discontinuously.

20 28. Composition according to Claims 18 to 27, characterized in that it comprises a vehicle which is pharmaceutically acceptable for an injectable formulation.

25 29. Composition according to Claims 18 to 27, characterized in that it comprises a vehicle which is pharmaceutically acceptable for application to the skin and/or mucous membranes.



30. Use of a transfer agent as defined in Claims 1 to 17, for manufacturing a medicinal product intended for treating diseases.

*Sub E*

31. Method for treating the human or animal body, comprising the following steps:

5 (1) bringing the nucleic acid into contact with a transfer agent as defined in Claims 1 to 17, so as to form a complex, and

(2) bringing the cells of the human or animal body into

10 contact with the complex formed in (1).

32. Method for transferring nucleic acids into cells, characterized in that it comprises the following steps:

(1) bringing the nucleic acid into contact with a

15 transfer agent as defined, so as to form a complex, and

(2) bringing the cells into contact with the complex formed in (1).

33. Method for transferring nucleic acids into cells according to Claims 31 or 32, characterized

20 in that said transfer agent and/or said nucleic acid are mixed beforehand with one or more adjuvant(s) as defined in Claims 22 to 27.

*add E3*